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| 10/579,711 | 02/27/2007 | Kara Calhoun | STAN-337 | 4793 |

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| EXAMINER | |
|---|---|
| UNDERDAHL, THANE E | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1651 | |

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/579,711 | CALHOUN ET AL. | |
| | Examiner | Art Unit | |
| | THANE UNDERDAHL | 1651 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *16 January 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *18 May 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1/3/07*
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

**Detailed Action**

This Office Action is in response to the Applicant's reply received 1/16/08. Claims 1-18 are pending. No Claims are withdrawn. No Claims are cancelled. No Claims have been amended. No Claims are new. Claims 1-18 are considered in this Office Action.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 8 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "nucleoside monophosphates" is unclear since phosphated nucleosides are defined as nucleotides (supported by Biology-Online.com, Definition Nucleoside and Nucleotide). Clarification is required.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 3-8, 10-16 and 18 are rejected under 35 U.S.C. 102(b) as being anticipated by Swartz #1. (U.S. Patent # 6168931, 2001).

These claims are to a method for the synthesis of biological macromolecules in vitro comprising the following step:

- Synthesizing said biological macromolecules in a reaction mix including phosphate-free energy source in the presence of exogenous phosphate.

These claims further limit that the phosphate free energy source is pyruvate or glutamate. The phosphates such as potassium phosphate is present at a concentration of 1 mM to about 20 mM. Claim 7 limits that the phosphate source is released during the reaction. Claim 8 limits that the reaction mix comprises nucleoside monophosphates. Claims 10 and 11 limit the template for synthesizing the biological macromolecules. Claims 12 and 11 limit the reaction to a batch or continuous reaction respectively. Claims 14 and 15 limit the E. coli extract comprising the reaction mix. Claims 16 limits the reaction mix to a magnesium concentration to about 5 mM to 10 mM. Claim 18 limits that the reaction mix comprises one or more of spermine, spermidine and putrescine.

Swartz #1 teach a method of synthesizing biological marcomolecules such as proteins (Figures 1 and 3) using a reaction mix comprising 200mM of glutamate, the nucletide monophosphate cAMP, **phosphoenol pyruvate** (**PEP**), 15 mM of $Mg(Ac)_2$ and a T7RNA polymerise to transcribe mRNA from a DNA plasmid for subsequent protein translation using an E. coli S30 extract (col 9, lines 34-41). E.coli S30 extract is the same bacteria extract describe in the Applicant's specification (paragraph 53). Swartz #1 also teach that if pyruvate is used as an energy source then the PEP is removed for the reaction mix and replaced with 32 mM of pyruvate and 6.7 mM of

potassium phosphate (col 9, lines 43-48). Swartz #1 teach that a phosphate source is released and recycled during the reaction (Fig 1A and 1B, where "Pi" is the abbreviation for inorganic phosphate). Their method can be performed continuously or batch-wise (col 6, lines 25-30). They also teach their reaction mix can comprise spermine or spermidine (col 6, lines 49-50).

Therefore the references anticipate claims 1, 3-8, 10-16 and 18.

Claims 1-8, 10-16 and 18 are rejected under 35 U.S.C. 102(b) as being anticipated by Swartz #2. (U.S. Patent # 6337191, January 2002).

The descriptions of claims 1, 3-8, 10-16 and 18 are recited in the 35 U.S.C § 102 rejection over Swartz #1 above and will not be repeated. Claim 2 limits that the energy source is glucose.

Swartz #2 teach a method of synthesizing biological macromolecules such as proteins (abstract) using a reaction mix comprising 200mM of glutamate, the nucletide monophosphate cAMP, PEP, 15 mM of $Mg(Ac)_2$ and a T7RNA polymerise to transcribe mRNA from a DNA plasmid for subsequent protein translation using an E. coli S30 extract (col 11, lines 20-30) which is the same bacterial extract describe in the Applicant's (paragraph 53). Swartz #2 also teach that if pyruvate is used as an energy source then the PEP is removed for the reaction mix and replaced with 33 mM of pyruvate and 6.7 mM of potassium phosphate (col 9, lines 43-48). Swartz #2 teach that other energy sources such as glucose can be used as well (Abstract). Swartz #2 teach that a phosphate source is released and recycled during the reaction (col 4, lines 1-5).

Their method can be performed continuously or batch-wise (col 5, lines 50-52). They also teach their reaction mix can comprise spermine or spermidine (col 8, lines 18-19).

Therefore the references anticipate claims 1-8, 10-16 and 18.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 3-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Swartz #1 as applied to 1, 3-8, 10-16 and 18 to the above 102 (b) rejection and for the following rationale.

The descriptions of claims 1, 3-8, 10-16 and 18 are recited in the 35 U.S.C § 102 rejection above and are applied here as well. Claim 9 excludes exogenous nucleotide triphosphates from the reaction mix. Claim 17 limits that the reaction mix is substantially free of polyethylene glycol.

Concerning claim 9. Initially Swartz#1 teach that the translation of RNA into polypeptides (Swartz#1, col 6, line 16) specifically the direct translation of mRNA to produce proteins (Swartz#1, col 6, lines 30-40). One of ordinary skill in the art would recognize that if the protein was directly translated from mRNA then, except for ATP, no exogenous **nucleotide triphosphates (NTP)** would be needed because protein synthesis does not require them since NTPs are necessary for DNA replication or RNA

transcription but not protein translation. Swartz#1 clearly teach that ATP is required for the ADP/ATP redox cycle which mediates the energy for the protein translation (Swartz#1, Figure 1). However since this ADP/ATP is a cyclic reaction then one of ordinary skill in the art would recognize by looking at Figure 1 of Swartz#1 that if the reaction was initiated with the appropriate starting materials such as phosphoenol pyruvate, pyruvate kinase with ADP that the reaction would flow to generate ATP that is recycled back to ADP via the translation process as shown in the diagram of Fig 1A of Swartz#1 which is copied below.


FIG. 1A

Therefore one of ordinary skill in the art would recognize that ADP could be substituted for ATP in the starting reaction mix and protein translation would still occur based on ATP/ADP being a reversible and cyclic process. A simple substitution one known element (ADP) for another (ATP) is obvious when both will predictably lead to the same result (protein translation) ((KSR Int'l Co. v. Teleflex, Inc. 550 U.S. 398 (2007), Section A, pg 14). Therefore it would be obvious for one of ordinary skill in the art to remove all NTPs from the system and not use any exogenous NTPs if mRNA was use as the template for protein translation.

Concerning claim 17. While Swartz#1 teaches polyethylene glycol in their reaction mix they also teach alternatives such as dextran, diethyl aminoethyl,

quaternary aminoethyl and aminoethyl (col 6, lines 54-55). M.P.E.P. § 2173.05(i) states "If alternative elements are positively recited in the specification, they may be explicitly excluded in the claims". Therefore since Swarz#1 teaches an alternative to polyethylene glycol then it would be obvious to exclude it via substituting it for another listed compound since they are known for the same purpose (M.P.E.P. § 2144.06).

Therefore claims 1, 3-8, 10-18 are obvious in view of the above references.

Claims 1-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Swartz #2 as applied to 1-8, 10-16 and 18 to the above 102 (b) rejection and for the following rationale and in light of Figure 1A of Swartz#1.

The descriptions of claims 1-8, 10-16 and 18 are recited in the 35 U.S.C § 102 rejection above and are applied here as well. Claim 9 excludes exogenous nucleotide triphosphates from the reaction mix. Claim 17 limits that the reaction mix is substantially free of polyethylene glycol.

Concerning claim 9. Initially Swartz#2 teach that the translation of RNA into polypeptides, specifically the direct translation of mRNA to produce proteins (Swartz#2, col 7, lines 66-67). One of ordinary skill in the art would recognize that if the protein was directly translated from mRNA then, except for ATP, no exogenous NTPs would be needed since protein synthesis does not require them. Swartz#2 clearly teach that ATP is required for the ADP/ATP redox cycle that mediates the energy for the protein translation (Swartz#2, Example 1). Example 1 of Swartz#2 is the same reaction that is diagrammed in Fig 1A of Swartz#1 above. As with Swartz#1, since this ADP/ATP is a

cyclic reaction then one of ordinary skill in the art would recognize by looking at Figure 1 of Swartz#1 that if the reaction was initiated with the appropriate starting materials such as phosphoenol pyruvate, pyruvate kinase with ADP that the reaction would flow to generate ATP that would then recycle back to ADP via the translation process.

Therefore one of ordinary skill in the art would recognize that ADP could be substituted for ATP in the starting reaction mix and protein translation would still occur based on ATP/ADP being a reversible and cyclic process. It is obvious that a simple substitution one known element (ADP) for another (ATP) is obvious when both will predictably lead to the same result (protein translation) ((KSR Int'l Co. v. Teleflex, Inc. 550 U.S. 398 (2007), Section A, pg 14). Therefore it would be obvious for one of ordinary skill in the art to remove all NTPs from the system and not use any exogenous NTPs if mRNA was use as the template for protein translation.

Concerning claim 17. While Swartz#2 teaches polyethylene glycol in their reaction mix they also teach alternatives such as dextran, diethyl aminoethyl, quaternary aminoethyl and aminoethyl (col 8, lines 23-25). M.P.E.P. § 2173.05(i) states "If alternative elements are positively recited in the specification, they may be explicitly excluded in the claims". Therefore since Swarz#2 teaches an alternative to polyethylene glycol then it would be obvious to exclude it via substituting it for another listed compound since they are known for the same purpose (M.P.E.P. § 2144.06).

Therefore claims 1-18 are obvious in view of the above references.

No claims are currently allowed in this application.

**In response to this office action the applicant should specifically point out the support for any amendments made to the disclosure**, including the claims (MPEP 714.02 and 2163.06). Due to the procedure outlined in MPEP § 2163.06 for interpreting claims, it is noted that other art may be applicable under 35 U.S.C. § 102 or 35 U.S.C. § 103(a) once the aforementioned issue(s) is/are addressed.

Applicant is requested to provide a list of all copending U.S. applications that set forth similar subject matter to the present claims. A copy of such copending claims is requested in response to this Office action.

CONTACT INFORMATION

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Thane Underdahl whose telephone number is (571) 272-9042. The examiner can normally be reached Monday through Thursday, 8:00 to 17:00 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached at (571) 272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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